

REMARKS

In view of the following remarks, the Examiner is requested to allow Claims 1-2, 5-25, 27-40, and 102-165, the only claims pending and under examination in this application.

Claims 6 and 148 have been amended to correct minor informalities. No new matter has been added. As no new matter has been added by way of this amendment, entry thereof by the Examiner is respectfully requested.

Claim Objections

Claims 6 and 148 were objected to because of minor informalities. As indicated above, Claims 6 and 148 have been amended to correct these minor informalities. Consequently, this objection may be withdrawn.

Claim Rejections – 35 U.S.C. § 103

Claims 1, 10, 15-22, 37, 39-40, 122, 124, 126-132, and 139-145 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Southern et al. (*Nucleic Acids Research*, 1994, vol. 22, pp. 1368-73) (hereinafter "Southern (1994)"), in view of Southern (*Current Opinions in Biotechnology*, 1996, vol. 7, pp. 85-88) (hereinafter "Southern (1996)"), in view of Drmanac et al. (*Genomics*, 1989, vol. 4, pp. 114-28).

In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must first demonstrate that the combined prior art references teach or suggest all the claimed limitations. *See Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342 (Fed. Cir. 2007) ("the burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make [every element of] the composition or device, or carry out the [entire] claimed process, and would have had a reasonable expectation of success in doing so," (*citing KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007))); and see *Omegaflex, Inc. v. Parker-Hannifin Corp.*, 2007 U.S. App. LEXIS 14308 (Fed. Cir. 2007) ("[t]he Supreme Court recently explained that 'a patent

composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art," (*citing KSR Int'l Co.* at 1741)); and see *Dystar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006) ("[once] all claim limitations are found in a number of prior art references, the factfinder must determine '[w]hat the prior art teaches, whether it teaches away from the claimed invention, and whether it motivates a combination of teachings from different references,'" (*citing In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004))).

Independent Claims 1, 102, and 122 are directed to computer based methods for selecting a hybridization oligonucleotide to hybridize to a target nucleotide sequence. Independent Claims 1, 102, and 122 include the elements of: (b) determining and evaluating for each of said oligonucleotides at least one parameter that is predictive of the ability of each of said oligonucleotides to hybridize to said target nucleotide sequence, wherein said determining and evaluating are performed using an algorithm under computer control; (c) selecting a subset of oligonucleotides within said predetermined number of non-identical oligonucleotides based on an examination of said parameter; (d) identifying oligonucleotides in said subset that are in clusters along a region of said nucleotide sequence that is hybridizable to said target nucleotide sequence; and (e) selecting, for a cluster of step (d), a hybridization oligonucleotide wherein the hybridization of said hybridization oligonucleotide is predicted by the presence of said hybridization oligonucleotide in said cluster.

In maintaining the rejection and in response to the Applicants' prior amendments and arguments, the Examiner alleges that the MPEP states:

In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) (Appellant argued that claims to a permanent mold casting apparatus for molding trunk pistons were allowable over the prior art because the claimed invention combined "old permanent-mold structures together with a timer and solenoid which automatically actuates the known pressure valve system to release the inner core after a predetermined time has elapsed." The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.).

Office Action, pg. 7, last paragraph, citing MPEP § 2144.04(III). The Applicants respectfully submit that the above cited reference to *In re Venner* is

inapplicable to the instant case because *In re Venner* deals with "providing an automatic or mechanical means to replace a manual activity", which is not the same as the Applicants' claimed invention. Here, the Applicants claim a computer based method for selecting a hybridization oligonucleotide to hybridize to a target sequence. In contrast, as set forth above, in *In re Venner*, the appellant contended that his invention was in "a timer and solenoid which automatically actuates the known pressure valve system to release the inner core after a predetermined time has elapsed." *In re Venner*, 262 F.2d at 94 (emphasis added). Thus, in *In re Venner*, the appellant's invention, although performed automatically, still resulted in the physical performance of the method. As such, *In re Venner* does not deal with computer based methods and has no bearing on the Applicants' instantly claimed invention.

In addition, the Examiner asserts that "it is obvious to automate a manual activity". Office Action, pg. 10, ¶ 3.

The Applicants respectfully disagree with the Examiner's position. Southern (1994) indicates that the disclosed array method "provides an empirical method for analyzing the interactions of a target molecule with a complete set of complementary oligonucleotides." Southern (1994), pg. 1373, Discussion, last sentence (emphasis added). Similar to Southern (1994), Southern (1996) only teaches or suggests empirical methods of observing oligonucleotide hybridization. See Southern (1996), pg. 85, Introduction; and pg. 86, col. 2, ¶ 3 to pg. 87, col. 2, first full paragraph. Consequently, neither Southern (1994) nor Southern (1996) discloses or suggests a computer based method for selecting a hybridization oligonucleotide to hybridize to a target nucleotide sequence.

In addition, Southern (1994) and Southern (1996) do not disclose or suggest that the determining and evaluating of parameters that are predictive of the ability of the oligonucleotides to hybridize to the target nucleotide sequence are performed using an algorithm under computer control.

The Applicants respectfully submit that the Examiner's assertion that "it is obvious to automate a manual activity" is insufficient to maintain a *prima facie* case of obviousness against the present claims. Automation of an empirical method, as the Examiner suggests, would not result in a "computer based method . . . performed using an algorithm under computer control", as claimed by the Applicants. Rather, automation of an empirical method still results in an empirical method. The method may be performed automatically, but it is an empirical method nonetheless.

Thus, the cited references in no way disclose or suggest a computer based method for selecting a hybridization oligonucleotide to hybridize to a target nucleotide sequence.

In addition, the cited references do not disclose or suggest that the determining and evaluating of parameters that are predictive of the ability of the oligonucleotides to hybridize to the target nucleotide sequence are performed using an algorithm under computer control.

Consequently, a *prima facie* case of obviousness cannot be maintained and this rejection may be withdrawn.

Additionally, the Examiner alleges that Figures 3 and 4 of Southern (1994) illustrate a "rung darkness" parameter that represents hybridization intensity. Office Action, pg. 4-5, bridging paragraph. The Examiner further alleges that Southern (1994), Figure 3c "illustrates (through numbers with arrows) selection and identification of specific oligonucleotides in the subsets that are hybridizable to the target nucleotide sequences". Office Action, pg. 5, lines 4-8. Thus, the Examiner is apparently equating Southern (1994), Figures 3 and 4, with the claimed elements of (c) selecting a subset of oligonucleotides within said predetermined number of non-identical oligonucleotides based on an examination of said parameter; and (d) identifying oligonucleotides in said subset that are in clusters along a region of said nucleotide sequence that is hybridizable to said target nucleotide sequence, as claimed by the Applicants.

In addition, the Examiner equates the disclosure in Southern (1996) on page 87, column 2, lines 4-7, of a “[c]omparison of the hybridization patterns of wild-type and mutant sequences to an array of oligonucleotides complementary to the wild-type” with the claimed element of “(e) selecting, for a cluster of step (d), a hybridization oligonucleotide wherein the hybridization of said hybridization oligonucleotide is predicted by the presence of said hybridization oligonucleotide in said cluster”. Office Action, pg. 6, ¶ 2.

The Applicants respectfully disagree. Southern (1994) is directed to a method for making “[a]rrays of oligonucleotides corresponding to a full set of complements of a known sequence . . . in a single series of base couplings in which each base in the complement is added in turn.” Southern (1994), pg. 1368, Abstract, first sentence (emphasis added). Moreover, Southern (1994) indicates that the disclosed array method “provides an empirical method for analyzing the interactions of a target molecule with a complete set of complementary oligonucleotides.” Southern (1994), pg. 1373, Discussion, last sentence (emphasis added). Furthermore, Southern (1996) merely discloses that “arrays are of two basically different types: general purpose arrays and dedicated arrays. General purpose arrays, comprising all sequences of a given length, can be used to analyze sequences for which no previous sequence information is available. Dedicated or ‘scanning’ arrays represent the oligonucleotides complementary target of known sequence.” Southern (1996), col. 2, last paragraph. Thus, similar to Southern (1994), nowhere does Southern (1996) disclose or suggest the selection of a subset of oligonucleotides.

As such, nowhere does Southern (1994) or Southern (1996) disclose or suggest the selection of a subset of oligonucleotides. Thus, Southern (1994) and Southern (1996) do not disclose or suggest the Applicants’ claimed elements of: (c) selecting a subset of oligonucleotides within said predetermined number of non-identical oligonucleotides based on an examination of said parameter; (d) identifying oligonucleotides in said subset that are in clusters along a region of said nucleotide sequence that is hybridizable to said target nucleotide sequence; and (e) selecting,

for a cluster of step (d), a hybridization oligonucleotide wherein the hybridization of said hybridization oligonucleotide is predicted by the presence of said hybridization oligonucleotide in said cluster.

Drmanac was cited solely for the disclosure of sequential overlapping oligomers of equal length. Office Action, pg. 7, ¶ 1. As such, Drmanac fails to remedy the deficiencies in Southern (1994) and Southern (1996) discussed above.

Consequently, the Applicants contend that the cited combination of references does not render Claims 1, 10, 15-22, 37, 39-40, 122, 124, 126-132, and 139-145 obvious and respectfully request that the 35 U.S.C. § 103(a) rejection be withdrawn.

Claims 2, 11-13, 102-104, 106-112, 119-121, 123, 146-151, and 153-156 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Southern (1994), in view of Southern (1996), in view of Drmanac, and further in view of Southern et al. (*Genomics*, 1992, vol. 13, pp. 1008-17) (hereinafter "Southern (1992)"). As set forth above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest a computer based method for selecting a hybridization oligonucleotide to hybridize to a target nucleotide sequence. In addition, the cited references do not disclose or suggest that the determining and evaluating of parameters that are predictive of the ability of the oligonucleotides to hybridize to the target nucleotide sequence are performed using an algorithm under computer control. Furthermore, as discussed above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest elements (c), (d), and (e) of the Applicants' claimed invention. Southern (1992) was cited solely for its alleged disclosure of a method of quantitative ranking. Consequently, Southern (1992) fails to remedy the deficiencies of Southern (1994), Southern (1996), and Drmanac. Therefore, the cited combination of references does not disclose or suggest all the elements of Claims 2, 11-13, 102-104, 106-112, 119-121, 123, 146-151, and 153-156, and the Applicants respectfully request withdrawal of this rejection.

Claims 5, 6, 23-24, 30-32, 105, 125, 133-136, 157, and 159-165 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Southern (1994), in view of Southern (1996), in view of Drmanac, and further in view of Petersheim et al. (*Biochemistry*, 1983, vol. 22, pp. 256-263). As set forth above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest a computer based method for selecting a hybridization oligonucleotide to hybridize to a target nucleotide sequence. In addition, the cited references do not disclose or suggest that the determining and evaluating of parameters that are predictive of the ability of the oligonucleotides to hybridize to the target nucleotide sequence are performed using an algorithm under computer control. Furthermore, as discussed above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest elements (c), (d), and (e) of the Applicants' claimed invention. Petersheim was cited solely for its alleged disclosure of thermodynamic parameters and cut-off values. Consequently, Petersheim fails to remedy the deficiencies of Southern (1994), Southern (1996), and Drmanac. Therefore, the cited combination of references does not disclose or suggest all the elements of Claims 5, 6, 23-24, 30-32, 105, 125, 133-136, 157, and 159-165, and the Applicants respectfully request withdrawal of this rejection.

Claims 105, 113-115, and 158 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Southern (1994), in view of Southern (1996), in view of Drmanac, in view of Southern (1992), and further in view of Petersheim. As set forth above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest a computer based method for selecting a hybridization oligonucleotide to hybridize to a target nucleotide sequence. In addition, the cited references do not disclose or suggest that the determining and evaluating of parameters that are predictive of the ability of the oligonucleotides to hybridize to the target nucleotide sequence are performed using an algorithm under computer control. Furthermore, as discussed above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest elements (c), (d), and (e) of the Applicants' claimed invention. Southern (1992) was cited solely for its alleged disclosure of a method of quantitative ranking. Petersheim was

cited solely for its alleged disclosure of thermodynamic parameters and cut-off values. Consequently, both Southern (1992) and Petersheim fail to remedy the deficiencies of Southern (1994), Southern (1996), and Drmanac. Therefore, the cited combination of references does not disclose or suggest all the elements of Claims 105, 113-115, and 158, and the Applicants respectfully request withdrawal of this rejection.

Claims 8-9 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Southern (1994), in view of Southern (1996), in view of Drmanac, and further in view of McMahon et al. (U.S. Patent No. 5,310,650). As set forth above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest a computer based method for selecting a hybridization oligonucleotide to hybridize to a target nucleotide sequence. In addition, the cited references do not disclose or suggest that the determining and evaluating of parameters that are predictive of the ability of the oligonucleotides to hybridize to the target nucleotide sequence are performed using an algorithm under computer control. Furthermore, as discussed above, Southern (1994), Southern (1996), and Drmanac are deficient in that they fail to disclose or suggest elements (c), (d), and (e) of the Applicants' claimed invention. McMahon was cited solely for its alleged disclosure of kinetic properties and coupling efficiencies. Consequently, McMahon fails to remedy the deficiencies of Southern (1994), Southern (1996), and Drmanac. Therefore, the cited combination of references does not disclose or suggest all the elements of Claims 8-9, and the Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10971464-3.

Respectfully submitted,

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